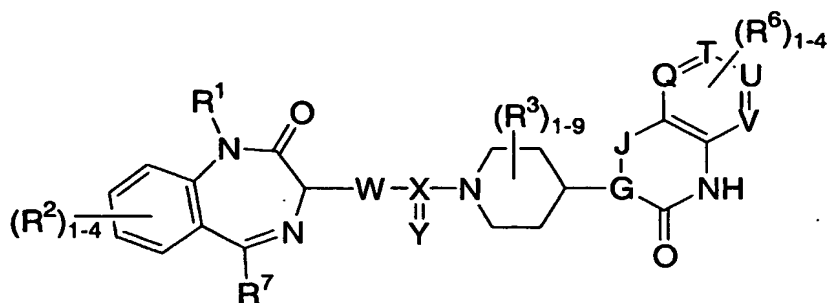


## WHAT IS CLAIMED IS:

1. A compounds of formula I:



wherein:

$R^1$  is selected from:

- 1) H,  $C_1$ - $C_6$  alkyl,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl,  $C_3$ -6 cycloalkyl, and heterocycle, unsubstituted or substituted with one or more substituents independently selected from:
  - a)  $C_1$ -6 alkyl,
  - b)  $C_3$ -6 cycloalkyl,
  - c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ,
  - d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ,
  - e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ,
  - f)  $(F)_p C_{1-3}$  alkyl,
  - g) halogen,
  - h)  $OR^4$ .
  - i)  $O(CH_2)_s OR^4$ .
  - j)  $CO_2R^4$ .
  - k)  $(CO)NR^{10}R^{11}$ .
  - l)  $O(CO)NR^{10}R^{11}$ .

- 5
- m)  $N(R^4)(CO)NR^{10}R^{11}$ ,
  - n)  $N(R^{10})(CO)R^{11}$ ,
  - o)  $N(R^{10})(CO)OR^{11}$ ,
  - p)  $SO_2NR^{10}R^{11}$ ,
  - q)  $N(R^{10})SO_2R^{11}$ ,
  - r)  $S(O)_mR^{10}$ ,
  - s) CN,
  - t)  $NR^{10}R^{11}$ ,
  - u)  $N(R^{10})(CO)NR^4R^{11}$ , and
  - 10 v)  $O(CO)R^4$ ; and
- 2) aryl or heteroaryl, unsubstituted or substituted with one or more substituents independently selected from:
- a)  $C_{1-6}$  alkyl,
  - 15 b)  $C_{3-6}$  cycloalkyl,
  - c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ,
  - d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ,
  - 20 e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ,
  - f)  $(F)_pC_{1-3}$  alkyl,
  - g) halogen,
  - h)  $OR^4$ ,
  - 25 i)  $O(CH_2)_sOR^4$ ,
  - j)  $CO_2R^4$ ,
  - k)  $(CO)NR^{10}R^{11}$ ,
  - l)  $O(CO)NR^{10}R^{11}$ ,
  - m)  $N(R^4)(CO)NR^{10}R^{11}$ ,
  - 30 n)  $N(R^{10})(CO)R^{11}$ ,
  - o)  $N(R^{10})(CO)OR^{11}$ ,
  - p)  $SO_2NR^{10}R^{11}$ ,
  - q)  $N(R^{10})SO_2R^{11}$ ,
  - r)  $S(O)_mR^{10}$ ,

- s) CN,
- t)  $\text{NR}^{10}\text{R}^{11}$ ,
- u)  $\text{N}(\text{R}^{10})(\text{CO})\text{NR}^4\text{R}^{11}$ , and
- v)  $\text{O}(\text{CO})\text{R}^4$ ; and

5

$\text{R}^2$  is independently selected from H and:

- 1)  $\text{C}_{1-6}$  alkyl,
- 2)  $\text{C}_{3-6}$  cycloalkyl,
- 10 3) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $\text{R}^4$ , the
- 4) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $\text{R}^4$ , where
- 5) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $\text{R}^4$ , where
- 15 6)  $(\text{F})_p\text{C}_{1-3}$  alkyl,
- 7) halogen,
- 8)  $\text{OR}^4$ ,
- 9)  $\text{O}(\text{CH}_2)_5\text{OR}^4$ ,
- 10)  $\text{CO}_2\text{R}^4$ ,
- 20 11)  $(\text{CO})\text{NR}^{10}\text{R}^{11}$ ,
- 12)  $\text{O}(\text{CO})\text{NR}^{10}\text{R}^{11}$ ,
- 13)  $\text{N}(\text{R}^4)(\text{CO})\text{NR}^{10}\text{R}^{11}$ ,
- 14)  $\text{N}(\text{R}^{10})(\text{CO})\text{R}^{11}$ ,
- 15)  $\text{N}(\text{R}^{10})(\text{CO})\text{OR}^{11}$ ,
- 25 16)  $\text{SO}_2\text{NR}^{10}\text{R}^{11}$ ,
- 17)  $\text{N}(\text{R}^{10})\text{SO}_2\text{R}^{11}$ ,
- 18)  $\text{S}(\text{O})_m\text{R}^{10}$ ,
- 19) CN,
- 20)  $\text{NR}^{10}\text{R}^{11}$ ,
- 30 21)  $\text{N}(\text{R}^{10})(\text{CO})\text{NR}^4\text{R}^{11}$ , and
- 22)  $\text{O}(\text{CO})\text{R}^4$ ;

$\text{R}^7$  is selected from:

- 1) H, C<sub>0</sub>-C<sub>6</sub> alkyl, C<sub>2</sub>-C<sub>6</sub> alkenyl, C<sub>2</sub>-C<sub>6</sub> alkynyl, C<sub>3</sub>-<sub>6</sub> cycloalkyl and heterocycle, unsubstituted or substituted with one or more substituents independently selected from:

- 5
- a) C<sub>1</sub>-<sub>6</sub> alkyl,
- b) C<sub>3</sub>-<sub>6</sub> cycloalkyl,
- c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- 10 d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- f) (F)<sub>p</sub>C<sub>1</sub>-  
3 alkyl,
- 15 g) halogen,
- h) OR<sup>4</sup>,
- i) O(CH<sub>2</sub>)<sub>s</sub>OR<sup>4</sup>,
- j) CO<sub>2</sub>R<sup>4</sup>,
- k) (CO)NR<sup>10</sup>R<sup>11</sup>,
- 20 l) O(CO)NR<sup>10</sup>R<sup>11</sup>,
- m) N(R<sup>4</sup>)(CO)NR<sup>10</sup>R<sup>11</sup>,
- n) N(R<sup>10</sup>)(CO)R<sup>11</sup>,
- o) N(R<sup>10</sup>)(CO)OR<sup>11</sup>,
- p) SO<sub>2</sub>NR<sup>10</sup>R<sup>11</sup>,
- 25 q) N(R<sup>10</sup>) SO<sub>2</sub>R<sup>11</sup>,
- r) S(O)<sub>m</sub>R<sup>10</sup>,
- s) CN,
- t) NR<sup>10</sup>R<sup>11</sup>,
- u) N(R<sup>10</sup>)(CO)NR<sup>4</sup>R<sup>11</sup>,
- 30 v) O(CO)R<sup>4</sup>; and

- 2) aryl or heteroaryl, unsubstituted or substituted with one or more substituents independently selected from:

- a) C<sub>1</sub>-<sub>6</sub> alkyl,

- b) C<sub>3-6</sub> cycloalkyl,
- c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- e) heterocycle, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- f) (F)<sub>p</sub>C<sub>1-3</sub> alkyl,
- g) halogen,
- h) OR<sup>4</sup>,
- i) O(CH<sub>2</sub>)<sub>s</sub>OR<sup>4</sup>,
- j) CO<sub>2</sub>R<sup>4</sup>,
- k) (CO)NR<sup>10</sup>R<sup>11</sup>,
- l) O(CO)NR<sup>10</sup>R<sup>11</sup>,
- m) N(R<sup>4</sup>)(CO)NR<sup>10</sup>R<sup>11</sup>,
- n) N(R<sup>10</sup>)(CO)R<sup>11</sup>,
- o) N(R<sup>10</sup>)(CO)OR<sup>11</sup>,
- p) SO<sub>2</sub>NR<sup>10</sup>R<sup>11</sup>,
- q) N(R<sup>10</sup>)SO<sub>2</sub>R<sup>11</sup>,
- r) S(O)<sub>m</sub>R<sup>10</sup>,
- s) CN,
- t) NR<sup>10</sup>R<sup>11</sup>,
- u) N(R<sup>10</sup>)(CO)NR<sup>4</sup>R<sup>11</sup>, and
- v) O(CO)R<sup>4</sup>;

R<sup>4</sup> is selected from: H, C<sub>1-6</sub> alkyl, (F)<sub>p</sub>C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, aryl, heteroaryl and benzyl, unsubstituted or substituted with halogen, hydroxy or C<sub>1-6</sub> alkoxy;

R<sup>5</sup> is independently selected from H, substituted or unsubstituted C<sub>1-6</sub> alkyl, C<sub>3-6</sub> cycloalkyl, aryl, heteroaryl, OR<sup>4</sup>, N(R<sup>4</sup>)<sub>2</sub>, CO<sub>2</sub>R<sup>4</sup> and (F)<sub>p</sub>C<sub>1-6</sub> alkyl;

W is O, NR<sup>4</sup> or C(R<sup>4</sup>)<sub>2</sub>;

X is C or S;

Y is O, (R<sup>4</sup>)<sub>2</sub>, NCN, NSO<sub>2</sub>CH<sub>3</sub> or NCONH<sub>2</sub>, or Y is O<sub>2</sub> when X is S;

R<sup>3</sup> is independently selected from H, substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl, CN and CO<sub>2</sub>R<sup>4</sup>;

5

R<sup>6</sup> is independently selected from H and:

- a) C<sub>1-6</sub> alkyl,
- b) C<sub>3-6</sub> cycloalkyl,
- 10 c) aryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- d) heteroaryl, unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from R<sup>4</sup>,
- e) heterocycle, unsubstituted or substituted with 1-5 substituents
- 15 where the substituents are independently selected from R<sup>4</sup>,
- f) (F)<sub>p</sub>C<sub>1-3</sub> alkyl,
- g) halogen,
- h) OR<sup>4</sup>.
- i) O(CH<sub>2</sub>)<sub>s</sub>OR<sup>4</sup>,
- 20 j) CO<sub>2</sub>R<sup>4</sup>,
- k) (CO)NR<sup>10</sup>R<sup>11</sup>,
- l) O(CO)NR<sup>10</sup>R<sup>11</sup>,
- m) N(R<sup>4</sup>)(CO)NR<sup>10</sup>R<sup>11</sup>,
- n) N(R<sup>10</sup>)(CO)R<sup>11</sup>,
- 25 o) N(R<sup>10</sup>)(CO)OR<sup>11</sup>,
- p) SO<sub>2</sub>NR<sup>10</sup>R<sup>11</sup>,
- q) N(R<sup>10</sup>)SO<sub>2</sub>R<sup>11</sup>,
- r) S(O)<sub>m</sub>R<sup>10</sup>,
- s) CN,
- 30 t) NR<sup>10</sup>R<sup>11</sup>,
- u) N(R<sup>10</sup>)(CO)NR<sup>4</sup>R<sup>11</sup>, and
- v) O(CO)R<sup>4</sup>;

$R^{10}$  and  $R^{11}$  are independently selected from: H,  $C_{1-6}$  alkyl,  $(F)_pC_{1-6}$  alkyl,  $C_{3-6}$  cycloalkyl, aryl, heteroaryl and benzyl, unsubstituted or substituted with halogen, hydroxy or  $C_1-C_6$  alkoxy, where  $R^{10}$  and  $R^{11}$  may be joined together to form a ring selected from: azetidiny, pyrrolidiny, piperidiny, piperaziny and morpholiny, which is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from  $R^4$ ;

G-J is selected from: N,  $N-C(R^5)_2$ ,  $C=C(R^5)$ ,  $C=N$ ;  $C(R^5)$ ,  $C(R^5)-C(R^5)_2$ ,  $C(R^5)-C(R^5)_2-C(R^5)_2$ ,  $C=C(R^5)-C(R^5)_2$ ,  $C(R^5)-C(R^5)=C(R^5)$ ,  $C(R^5)-C(R^5)_2-N(R^5)$ ,  $C=C(R^5)-N(R^5)$ ,  $C(R^5)-C(R^5)=N$ ,  $C(R^5)-N(R^5)-C(R^5)_2$ ,  $C=N-C(R^5)_2$ ,  $C(R^5)-N=C(R^5)$ ,  $C(R^5)-N(R^5)-N(R^5)$ ,  $C=N-N(R^5)$ ,  $N-C(R^5)_2-C(R^5)_2$ ,  $N-C(R^5)=C(R^5)$ ,  $N-C(R^5)_2-N(R^5)$ ,  $N-C(R^5)=N$ ,  $N-N(R^5)-C(R^5)_2$  and  $N-N=C(R^5)$ ;

Q, T, U and V are each independently a carbon atom or a nitrogen atom wherein at least one but no more than three of Q, T, U and V are nitrogen atoms, and wherein when any of Q, T, U, or V is a carbon atom it is unsubstituted or substituted where the substituents are independently selected from  $R^6$ ;

p is 0 to  $2q+1$ , for a substituent with q carbons;

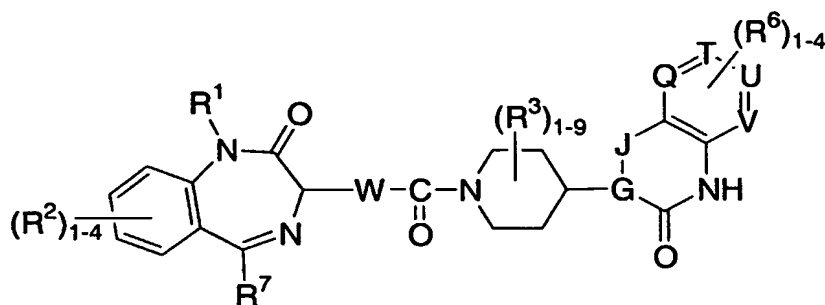
m is 0, 1 or 2;

n is 0 or 1;

s is 1, 2 or 3;

and pharmaceutically acceptable salts and individual diastereomers thereof.

2. The compound of claim 1 of the formula Ia:



and pharmaceutically acceptable salts and individual diastereomers thereof.

5

3. The compound of claim 2, wherein R<sup>7</sup> is phenyl, unsubstituted or substituted with one or substituents independently selected from:

10

- a) C<sub>1-6</sub> alkyl,
- b) OH,
- c) OR<sup>5</sup>,
- d) halogen,
- e) CO<sub>2</sub>R<sup>4</sup>,
- f) S(O)<sub>m</sub>R<sup>5</sup>,
- g) N(R<sup>4</sup>)<sub>2</sub>, and
- j) CN,

15

20 and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of claim 2, wherein R<sup>7</sup> is heteroaryl, unsubstituted or substituted with one or substituents independently selected from:

25

- a) C<sub>1-6</sub> alkyl,
- b) OH,
- c) OR<sup>5</sup>,



- d) halogen,
- e)  $\text{CO}_2\text{R}^4$ ,
- f)  $\text{S}(\text{O})_m\text{R}^5$ ,
- g)  $\text{N}(\text{R}^4)_2$ , and
- 5 j) CN,

and pharmaceutically acceptable salts and individual diastereomers thereof.

10 5. The compound of claim 2, wherein  $\text{R}^7$  is selected from H and  $\text{C}_1$ - $\text{C}_6$  alkyl,  $\text{C}_1$ - $\text{C}_6$  alkenyl,  $\text{C}_1$ - $\text{C}_6$  alkynyl,  $\text{C}_3$ - $\text{C}_6$  cycloalkyl, unsubstituted or substituted with one or substituents independently selected from:

- a)  $\text{C}_{1-6}$  alkyl,
- 15 b)  $\text{C}_{1-6}$  alkoxy,
- c) fluorine,
- d) HO,
- e)  $\text{OR}^5$ ,
- f)  $\text{CO}_2\text{R}^4$ ,
- 20 g)  $\text{CON}(\text{R}^4)_2$ ,
- h)  $\text{S}(\text{O})_m\text{R}^5$ , and
- i)  $\text{N}(\text{R}^4)_2$ ; and

and pharmaceutically acceptable salts and individual diastereomers thereof.

25

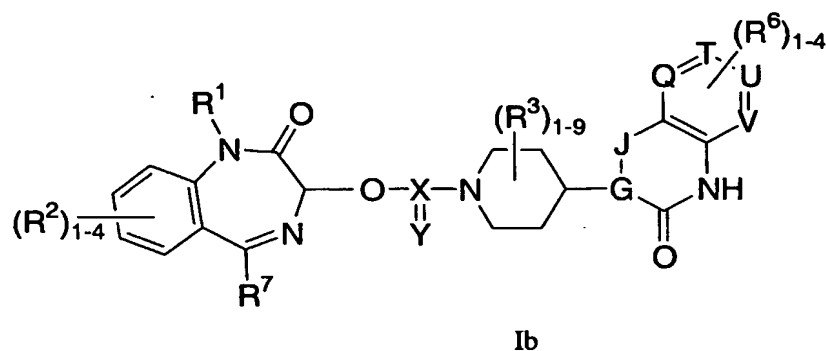
6. The compound of claim 2, wherein  $\text{R}^7$  is heterocycle, unsubstituted or substituted with one or substituents independently selected from:

- a)  $\text{C}_{1-6}$  alkyl,
- 30 b)  $\text{C}_{1-6}$  alkoxy,
- c) fluorine,
- d) HO,
- e)  $\text{OR}^5$ ,
- f)  $\text{CO}_2\text{R}^4$ ,

- g)  $\text{CON}(\text{R}^4)_2$ ,
- h)  $\text{S}(\text{O})_m\text{R}^5$ , and
- i)  $\text{N}(\text{R}^4)_2$ ; and

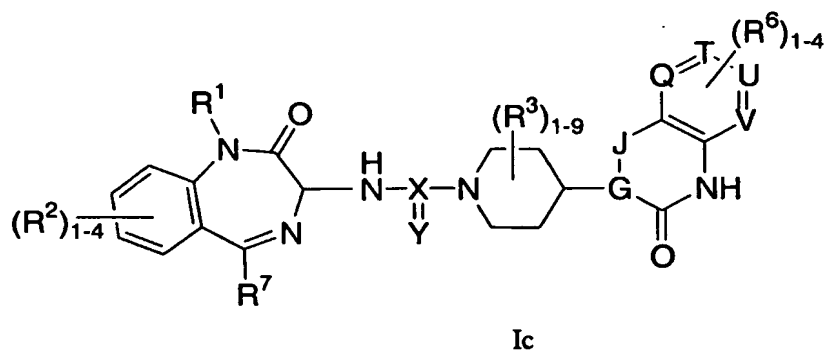
5 and pharmaceutically acceptable salts and individual diastereomers thereof.

10 7. The compound of claim 1 of the formula Ib:



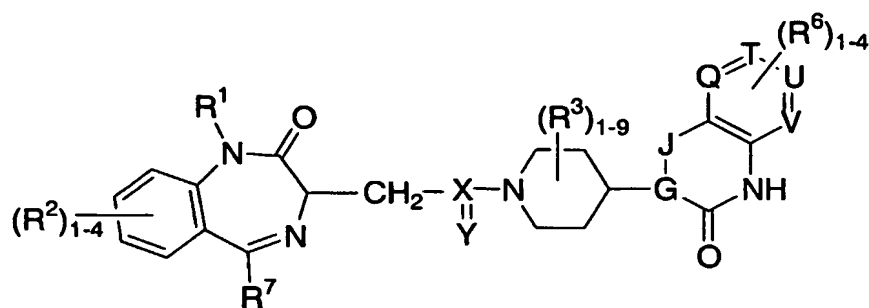
and pharmaceutically acceptable salts and individual diastereomers thereof.

15 8. The compound of claim 1 of the formula Ic:



and pharmaceutically acceptable salts and individual diastereomers thereof.

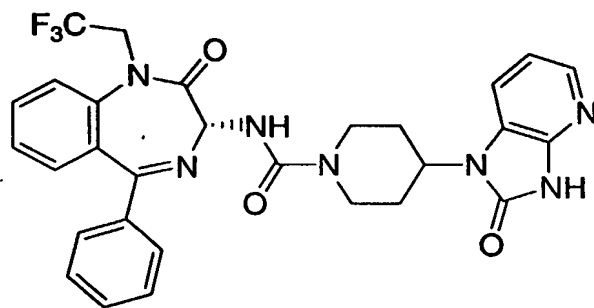
9. The compound of claim 1 of the formula Id:

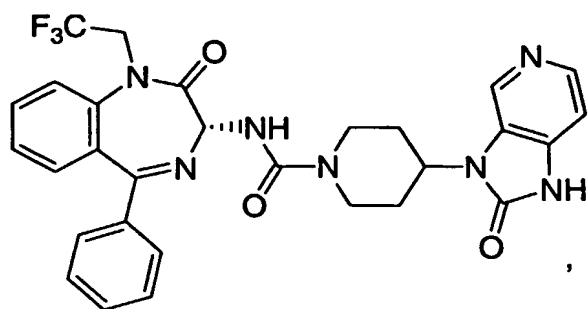
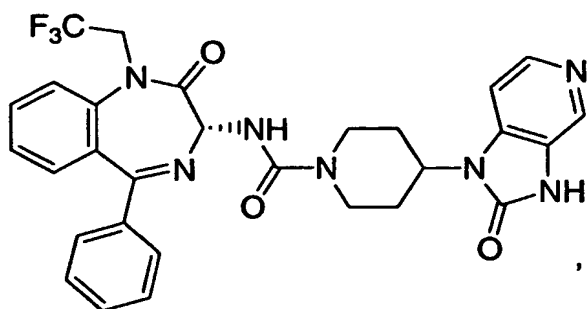


Id

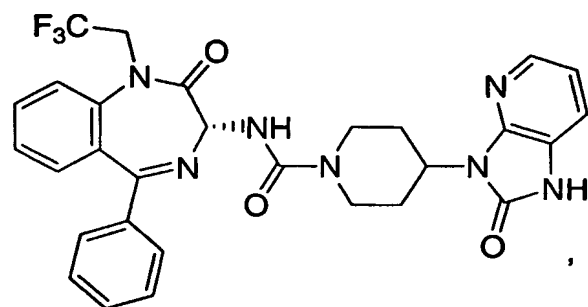
and pharmaceutically acceptable salts and individual diastereomers thereof.

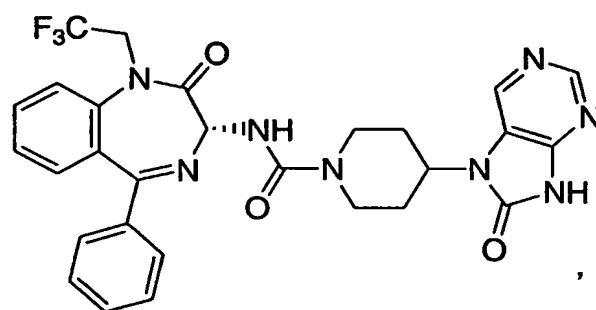
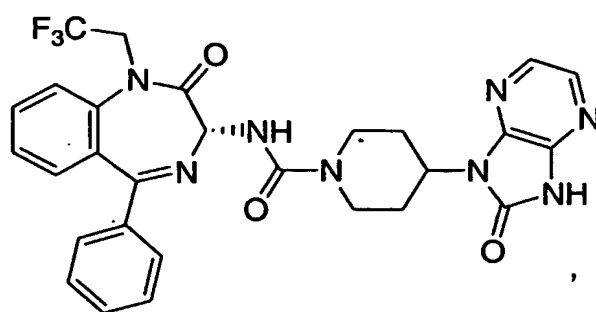
10. A compound selected from:



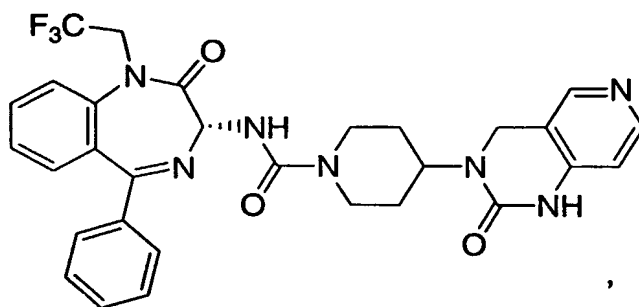


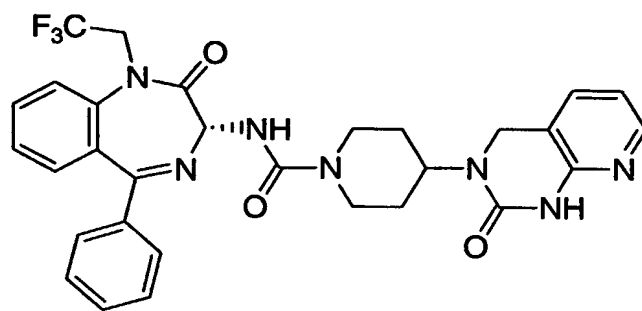
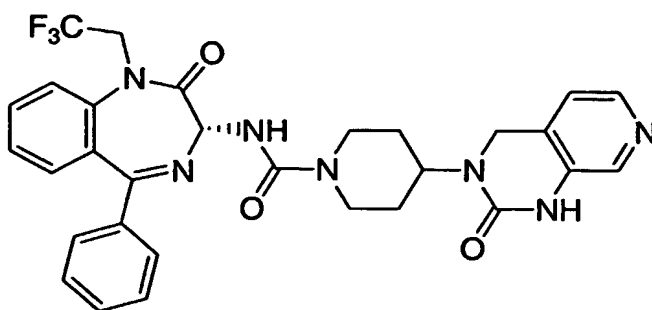
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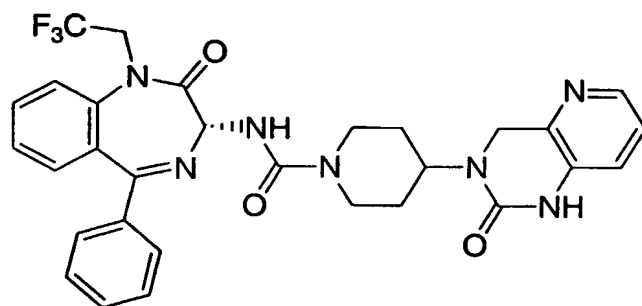


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5



and pharmaceutically acceptable salts and individual diastereomers thereof.

10

11. A pharmaceutical composition which comprises an inert carrier and the compound of Claim 1.

12. A method for antagonism of CGRP receptor activity in a mammal which comprises the administration of an effective amount of the compound of Claim 1.

5 13. A method for treating, controlling, ameliorating or reducing the risk of headache, migraine or cluster headache in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of the compound of Claim 1.

10 14. A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

15 a therapeutically effective amount of a second agent selected from serotonin agonists, analgesics, anti-inflammatory agents, anti-hypertensives and anticonvulsants.

15. The method of claim 14, wherein said second agent is selected from a  $5HT_{1B/1D}$  agonist, a  $5HT_{1D}$  agonist, and a  $5HT_{1F}$  agonist.

20 16. The method of claim 15, wherein said second agent is selected from rizatriptan, sumatriptan, naratriptan, zolmitriptan, almotriptan, eletriptan, avatriptan, frovatriptan, LY334370 and PNU-142633.

25 17. The method of claim 14, wherein said second agent is selected from ergotamine and dihydroergotamine.

18. The method of claim 14, wherein said second agent is aspirin or acetaminophen.

30 19. The method of claim 14, wherein said second agent is a glucocorticoid.

20. The method of claim 14, wherein said second agent is a non-steroidal anti-inflammatory agent.

21. The method of claim 20, wherein said second agent is selected from ibuprofen, ketoprofen, fenoprofen, naproxen, indomethacin, sulindac, meloxicam, piroxicam, tenoxicam, lornoxicam, ketorolac, etodolac, mefenamic acid, meclofenamic acid, flufenamic acid, tolfenamic acid, diclofenac, oxaprozin, apazone, nimesulide, nabumetone, tenidap, etanercept, tolmetin, phenylbutazone, oxyphenbutazone, diflunisal, salsalate, olsalazine and sulfasalazine.

22. The method of claim 14, wherein said second agent is an anticonvulsant selected from topiramate, zonisamide, divalproex sodium, pregabalin, gabapentin, levetiracetam, lamotrigine and tiagabine.

23. The method of claim 14, wherein said second agent is an anti-hypertensive selected from angiotensin II antagonists, angiotensin I antagonists, angiotensin converting enzyme inhibitors, and renin inhibitors.

24. The method of claim 23, wherein said second agent is selected from losartan, candesartan, candesartan cilexetil, irbesartan, valsartan, eprosartan, telmisartan, olmesartan, medoxomil, captopril, benazepril, quinapril, perindopril, ramipril, trandolapril, lisinopril, and enalapril

25. A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from anti-anxiety agents and neuroleptics.

26. The method of claim 25, wherein said second agent is selected from, diazepam, alprazolam, chlordiazepoxide, olanzapine, droperidol, prochlorperazine, chlorpromazine and quetiapine.

27. A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and



a therapeutically effective amount of a second agent selected from beta-blockers and calcium channel blockers.

5                   28.     The method of claim 27, wherein said second agent is selected from timolol, propanolol, atenolol, metoprolol, nadolol, flunarizine, diltiazem, amlodipine, felodipine, nisolipine, isradipine, nimodipine, lomerizine, verapamil, nifedipine, prochlorperazine and civamide.

10                   29.     A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

15                   a therapeutically effective amount of a second agent selected from anti-depressants, selective serotonin reuptake inhibitors, and NE reuptake inhibitors.

20                   30.     The method of claim 29, wherein said second agent is selected from amitriptyline, nortriptyline, clomipramine, imipramine, venlafaxine, doxepin, protriptyline, desipramine, trimipramine, fluoxetine, paroxetine, sertraline, duloxetine, escitalopram, and citalopram.

                  31.     A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

25                   a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from botulinum toxins A or B.

30                   32.     A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from vanilloid receptor antagonists, adenosine 1 antagonists, NR2B antagonists, substance P antagonists, granzyme B inhibitors, endothelin antagonists, norepinephrin precursors, nitric oxide synthase inhibitors, neuroleptics, bradykinin antagonists, gap junction inhibitors, AMPA/KA antagonists, sigma receptor agonists, chloride channel enhancers, monoamine oxidase inhibitors, opioid agonists, and leukotriene receptor antagonists.

33. The method of claim 32, wherein said second agent is selected from montelukast and zafirlukast.

34. The method of claim 32, wherein said second agent is aprepitant.

35. A method of treating or preventing migraine headaches, cluster headaches, and headaches, said method comprising the co-administration, to a person in need of such treatment, of:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from the group consisting of anti-emetics, prokinetics, and histamine H1 antagonists.

36. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from serotonin agonists, analgesics, anti-inflammatory agents, and anticonvulsants.

37. The composition of claim 36, wherein said second agent is selected from a  $5HT_{1B/1D}$  agonist, a  $5HT_{1D}$  agonist, and a  $5HT_{1F}$  agonist.

38. The composition of claim 37, wherein said second agent is selected from rizatriptan, sumatriptan, naratriptan, zolmitriptan, almotriptan, eletriptan, avitriptan, frovatriptan, LY334370 and PNU-142633.

5 39. The composition of claim 36, wherein said second agent is selected from ergotamine and dihydroergotamine.

40. The composition of claim 36, wherein said second agent is aspirin or acetaminophen.

10 41. The composition of claim 36, wherein said second agent is a glucocorticoid.

42. The composition of claim 36, wherein said second agent is a non-steroidal anti-inflammatory agent.

15 43. The composition of claim 42, wherein said second agent is selected from ibuprofen, ketoprofen, fenoprofen, naproxen, indomethacin, sulindac, meloxicam, piroxicam, tenoxicam, lornoxicam, ketorolac, etodolac, mefenamic acid, meclofenamic acid, flufenamic acid, tolfenamic acid, diclofenac, oxaprozin, apazone, nimesulide, nabumetone, tenidap, etanercept, tolmetin, phenylbutazone, oxyphenbutazone, diflunisal, salsalate, olsalazine and sulfasalazine.

20 44. The composition of claim 36, wherein said second agent is an anticonvulsant selected from topiramate, zonisamide, divalproex sodium, pregabalin, gabapentin, levetiracetam, lamotrigine and tiagabine.

25 45. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

30 a therapeutically effective amount of a second agent selected from angiotensin II antagonists, angiotensin I antagonists, angiotensin converting enzyme inhibitors, and renin inhibitors.

46. The composition of claim 45, wherein said second agent is selected from losartan, candesartan, candesartan cilexetil, irbesartan, valsartan, eprosartan, telmisartan, olmesartan, medoxomil, captopril, benazepril, quinapril, perindopril, ramipril, trandolapril, lisinopril, and enalapril.

- 5                   47. A pharmaceutical composition comprising:
- a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and
- 10 a therapeutically effective amount of a second agent selected from anti-anxiety agents and neuroleptics.

48. The composition of claim 47, wherein said second agent is selected from, diazepam, alprazolam, chlordiazepoxide, olanzapine, droperidol, prochlorperazine, chlorpromazine and quetiapine.

- 15                   49. A pharmaceutical composition comprising:
- a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and
- 20 a therapeutically effective amount of a second agent selected from beta-blockers and calcium channel blockers.

50. The composition of claim 49, wherein said second agent is selected from
- 25 timolol, propanolol, atenolol, metoprolol, nadolol, flunarizine, diltiazem, amlodipine, felodipine, nisolipine, isradipine, nimodipine, lomerizine, verapamil, nifedipine, prochlorperazine and civamide.

51. A pharmaceutical composition comprising:
- 30 a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and
- a therapeutically effective amount of a second agent selected from anti-depressants, selective serotonin reuptake inhibitors, and NE reuptake inhibitors.

52. The composition of claim 51, wherein said second agent is selected from amitriptyline, nortriptyline, clomipramine, imipramine, venlafaxine, doxepin, protriptyline, desipramine, trimipramine, fluoxetine, paroxetine, sertraline, duloxetine, escitalopram, and citalopram.

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53. A pharmaceutical composition comprising:

a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

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a therapeutically effective amount of a second agent selected from botulinum toxins A or B.

54. A pharmaceutical composition comprising:

15 a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from vanilloid receptor antagonists, adenosine 1 antagonists, NR2B antagonists, substance P antagonists, granzyme B inhibitors, endothelin antagonists, norepinephrin precursors, nitric oxide synthase inhibitors, neuroleptics, bradykinin antagonists, gap junction inhibitors, AMPA/KA antagonists, sigma receptor agonists, chloride channel enhancers, monoamine oxidase inhibitors, opioid agonists, and leukotriene receptor antagonists.

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55. The composition of claim 54, wherein said second agent is selected from montelukast and zafirlukast.

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56. The composition of claim 54, wherein said second agent is aprepitant.

57. A pharmaceutical composition comprising:

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a therapeutically effective amount of the compound of claim 1 or a pharmaceutically acceptable salt thereof; and

a therapeutically effective amount of a second agent selected from the group consisting of anti-emetics, prokinetics, and histamine H1 antagonists.